Catecholamine-secreting paragangliomas of the base of the skull

Report of two cases


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Two cases of catecholamine-secreting paragangliomas of the base of the skull are described. The patients presented with uncontrollable hypertension and, after investigation, tumors were discovered in the regions of the glomus jugulare and pterygopalatine ganglion, respectively. After cardiovascular stabilization and tumor embolization, the tumors were surgically removed, with subsequent resolution of hypertension. The incidence of these tumors is discussed.

KEY WORDS • paraganglioma • pheochromocytoma • skull neoplasm

Paraganglia are composed of cells of neural crest origin distributed widely throughout the autonomic nervous system. Recognized sites of paraganglion tissue include the carotid artery, ciliary and vagal bodies, the aorta and its major branches, the glomus jugulare complex, the bladder, the para-adrenal area, and, most notably, the adrenal medulla. Functioning tumors of paraganglion tissue, of which the pheochromocytoma, or catecholamine-secreting adrenal intramedullary tumor is the best known, may be responsible for uncontrollable hypertension. Tumor localization techniques reveal that 93% of these functional tumors are found in the adrenal medulla, with the other 7% occurring at sites along the aorta and its branches; tumors above the diaphragma sellae make up less than 1% of the total. These tumors may be clinically indistinguishable from pheochromocytomas, and identifying their position can be exceedingly difficult. Their location plays a crucial role in therapeutic considerations. We have recently treated two patients with a secreting tumor at the base of skull which was responsible for uncontrollable hypertension.

Case Reports

Case 1

This 39-year-old male laborer presented in March, 1984, with a 1-year history of hematospermia. He was admitted to a local hospital for cystoscopic investigation, where it was noted his blood pressure was 260/140 mm Hg.

Examination. His physical examination was otherwise normal. Cystoscopy was cancelled, and further screening investigations were carried out. Routine hematological and biochemical measurements were normal; however, a 24-hour urine collection revealed elevated catecholamine vanilmandelic acid (VMA) levels and urinary metanephrine. Abdominal computerized tomography (CT) and methyl-iodobenzyl guanidine (MIBG) scanning failed to demonstrate a tumor on two separate occasions; thus, the patient was transferred for further investigation.

A pentolinium-suppression test showed persistently elevated noradrenaline levels, with nonsuppression after intravenous injection of 5 mg pentolinium. Venous sampling for catecholamine analysis was undertaken and a marked noradrenaline gradient was noted at the level of both internal jugular veins. During the procedure, the patient became profoundly bradycardic, requiring external cardiac massage to maintain cardiac output. Thereafter, he underwent alpha- and beta-blockade with phenoxybenzamine (20 mg twice daily, later increased to 30 mg three times daily), and propranolol (10 mg three times daily), to prevent further cardiovascular instability.
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Subsequent CT scanning of the head and neck showed an expanded jugular foramen with destruction of the foramen magnum and erosion of the petrous apex (Fig. 1). Angiography revealed a hypervascular mass, filling from the left ascending pharyngeal, posterior auricular, and occipital arteries.

**Operations.** At surgery the tumor was found to fill the jugular foramen, extending down the jugular vein to 4 cm below the skull base. The jugular vein was occluded, and the tumor was embolized with lyophilized dura. During the procedure, the patient became asystolic, but responded to a single precordial thump. After an initial period of hypotension, he became severely hypertensive, and a sodium nitroprusside infusion was required for 24 hours to control his blood pressure. When he recovered from the anesthesia, it was noted that he had a left lower motor neuron facial palsy.

Four days after the embolization procedure, a combined neck dissection and posterior fossa craniectomy was performed with the patient in the park-bench position. A wide posterior auricular incision was made and the internal carotid artery, internal jugular vein, and the 10th, 11th, and 12th cranial nerves were identified and preserved. The seventh cranial nerve was identified at the stylomastoid foramen. The mastoid was drilled out and the sigmoid sinus exposed to the jugular bulb. After removal of the occipital bone over the lateral part of the left cerebellar hemisphere, the posterior fossa dura was opened; anterior to the exit of the ninth, 10th, and 11th cranial nerves, reddish discoloration of the tumor was seen. Inspection of the fifth and seventh through 11th cranial nerves and the petrosal venous system revealed no evidence of intradural tumor; therefore, attention was turned to the extradural space. The tumor was exenterated from the jugular foramen and was noted to extend anteriorly to the otic capsule, with medial extension and associated destruction of the clivus. Tumor involved both the jugular bulb and the internal jugular vein, which were removed. The sigmoid sinus was free of tumor. The ninth through 12th cranial nerves remained anatomically intact and, after hemostasis was achieved, the wound was closed in layers.

**Pathological Examination.** The tumor was composed of nests of cells with moderately pleomorphic round or oval nuclei and finely granular cytoplasm (Fig. 2). In the cytoplasm of most tumor cells were numerous small argyrophilic granules. Reticulin fibers surrounded the nests of cells. No mitoses were seen. The features were those of a paraganglioma.

**Postoperative Course.** The left facial nerve palsy remained, in association with glossopharyngeal and hypoglossal paralysis on the left side. This improved slowly, although it still had not returned to normal when the patient was last seen 6 months after surgery. Postoperative fluctuations in blood pressure were controlled with intermittent intravenous hydralazine. Urinary catecholamine levels were elevated postoperatively, but had settled to within normal limits by the time of discharge. A limited course of radiotherapy was given, and the patient remains normotensive without pharmacological therapy.

**Case 2**

This 35-year-old woman presented in November, 1985, with a 3-year-history of palpitations associated with hot flushes, headaches, and irritability. She was found to be hypertensive on routine physical examination in November, 1984, but no investigations were carried out then. Hypertension persisted, and she was sent for evaluation of her condition.

**Examination.** Screening investigations revealed elevated urinary VMA. Apart from an elevated blood pressure, the patient’s physical examination was normal. A pentolinium-suppression test showed a baseline
noradrenaline level of 6.52 ng/ml (normal 0.2 to 0.8 ng/ml) with nonsuppression after intravenous injection of 5 mg pentolinium. An MIBG was negative. Venous sampling showed markedly elevated levels of noradrenaline at the level of the internal jugular veins, predominant on the left side.

A CT scan of the head and neck failed to localize the tumor. Magnetic resonance imaging (MRI) revealed the presence of a homogeneous mass in the left pterygopalatine fossa (Fig. 3), which was subsequently evident on plain films of the maxillary sinuses. The mass invaded the posterolateral margin of the orbit and the posterior maxillary sinus, and extended upward into the middle cranial fossa. The greater wing of the sphenoid bone appeared to be eroded, with medial invasion of the lateral wall of the nasal cavity.

The patient’s blood pressure was controlled with alpha- and beta-blockade (phenoxybenzamine, 30 mg three times daily, and atenolol, 50 mg in the morning). She was transferred for further investigation. Carotid angiography showed that the tumor had a rich blood supply from the left maxillary artery (mainly via the accessory meningeal artery and the artery of the foramen rotundum), from the ascending pharyngeal artery, and from the cavernous segment of the internal carotid artery. No displacement of the internal carotid artery or invasion of the cavernous sinus was noted.

Operations. The tumor was embolized with lyophilized dura, and 2 days later was removed via a left lateral rhinotomy incision, continuing laterally to the infraorbital foramen. After removal of the anteromedial antral wall, the tumor was noted to be eroding through the posterior wall, but with no intracranial extension. The tumor was well demarcated; it stripped easily from the tissue planes and a total macroscopic removal was achieved.

Pathological Examination. The tumor consisted of cords and nests of cells separated by a fibrovascular stroma (Fig. 4). Tumor cells had dark round or oval nuclei and finely granular cytoplasm. The cytoplasmic granules stained positively with the argyrophil (Grimalius silver) and alkaline diazo methods. A modified Giemsa technique showed cytoplasmic chromaffin granules in the tumor tissue fixed in a dichromate (Zenker’s) fixative. No mitoses were seen. The features were those of a paraganglioma.

Electron microscopy showed numerous cytoplasmic dense granules (between 130 and 200 nm in diameter) situated centrally or eccentrically in single membrane-bound vacuoles (Fig. 5). A few poorly defined intercellular junctions were present.

Postoperative Course. The patient had no neurological deficit and remains normotensive without pharmacological intervention.

Discussion

Functional activity in extra-adrenal paragangliomas is rare. The possibility of catecholamine production by these tumors was discussed in the 1930’s by several authors, but was first observed by LeCompte in 1948, using extracts of carotid body tumor. It was not until 1964 that the presence of norepinephrine in considerable amounts in both carotid body tumors and a glomus jugulare tumor was confirmed. Later, both norepinephrine and epinephrine were demonstrated in carotid bodies and glomus jugulare tumors. In 1951, Terracol and Guerrier noted a marked increase in blood pressure during the removal of a glomus jugulare tumor, but it was Duke, et al., who reported in 1964 the first documented case of a catecholamine-secreting glomus jugulare tumor. Two years earlier, Berdal, et al., had reported the first documented case of a functional paraganglioma: a carotid body tumor for which the norepinephrine assay was highly positive. Further clinical reports followed, and by 1977 a total of 20 functioning paragangliomas had been reported. Of the 20, only eight were glomus tumors:
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Fig. 4. Case 2. Photomicrograph showing the excised tumor to be composed of nests and cords of cells in a fibrovascular stroma. H & E, x 175.

Fig. 5. Case 2. Electron micrograph of tumor tissue showing the cell cytoplasm with numerous dense core vesicles. x 35,000.

jugulare, tympanicum, or vagale. A further review in 1980 revealed a total of eight functioning glomus jugulare tumors, with the addition of one case report. To date, there have been 12 documented cases of functional glomus jugulare tumors,5-7,11,14-17,19,20,24 the majority of which have secreted predominately noradrenaline. There are no reported cases of functioning paragangliomas occurring in the pterygopalatine fossa. Although paragangliomas may occur anywhere in the body, their incidence above the diaphragm is less than 1%.17 We report here two cases of noradrenaline-secreting paragangliomas, confirmed both clinically and histologically. Both cases illustrate the need for thorough investigation of all possible sites of catecholamine-secreting tumors.22 Although the tumors occurred at the base of the skull, they presented with a clinical picture similar to that of a pheochromocytoma. With the aid of venous sampling, the tumors were localized to the head and neck region. Special investigations, including MRI, provided precise anatomical information. Preoperative alpha- and beta-blockade plus tumor embolization have made surgical removal of the tumors much easier than has been possible previously.

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